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DEPARTMENT OF THE ARMY
Fort Detrick
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IS IT POSSIBLE TO GROW VIRUSES

OUTSIDE OF CELLS?

By A. Cohen

Harefuah, Tel Aviv, Vol 65, VII, 1 Oct, 64, p 229

One of the first definitions of viruses says that unlike microbes they can only multiply in the cells of their hosts. It is clear today that this definition is not sufficient because there are small and filterable microorganisms that are not viruses but are intra-cellular parasites. For example -- the cause of the atypical pneumonia (PAP) was thought to be a virus till it was discovered that it is a parasitic microorganism belonging to the mycoplasma group (microbes without hard membrane) [1]. Today we can grow it in artificial cultures outside the host-cell. [2, 3].

According to Burnet's new definition [4] viruses are microorganisms whose diameter is smaller than 0.4 micron, that can multiply only in the living cells of a sensitive host, and the development of which includes an indispensable step of change into an ecliptic uncontagious form.

Microbes contain all or most of the enzymatic systems required for the use of the substrates as nourishment for their multiplication. Some groups which have lost these systems change into intra-cellular parasites. Microbes multiply by fission into two, and they always exist as whole morphological and functional units.

With viruses, which consist mainly of nucleic acid and protein, multiplication occurs in a different way. After the penetration of the virus particle into the host cell it disappears as a contagious, morphological unit and after a certain time (minutes to hours) many new virus particles appear in the cell. Multiplication of the viruses occurs therefore through multiplication of separate structural elements (nucleic

acid and protein, each separately) and then their final integration into whole particles that can be contagious. The instructions for this separate production are in the nucleic acid of the viruses -- which is sufficient for providing information for the creation of the whole virus in the host-cell. Experiments were made with nucleic acids of many viruses, and it was discovered in every case that they bring about the creation of whole viruses in the infected cells. [5].

There are a number of virus groups which in addition to nucleic acid and protein membrane (myxoviruses, poxviruses, herpes) also contain a lipoproteinic membrane; in their case it was not yet possible to produce whole viruses through penetration of nucleic acid alone.

Since methods were devised for producing specific proteins in systems containing ribosomes and RNA -- (RNA messenger) from a natural [6] or artificial [7] source, it was hypothesized that during contagion with the virus, their nucleic acid (RNA) serves as a substitute for the regular m-RNA of the cell and that it guides the cell's ribosomes in creating the cell's protein. Thus it was proven in practice that the nucleic acid of the tomato virus [8] or of the tobacco mosaic [9] or of the polio virus [10] can create specific proteins in vitro over ribosomes extracted from a microbe (that was totally unrelated to these viruses.)

In one experiment it was proven that nucleic acid of the virus EMC, encephalomyelocarditis of rodents, can create specific antigens of this virus when it is added to the suspension of ribosomes extracted from animal cells that are sensitive to EMC [11].

In another study the new nucleic acid of the tobacco mosaic virus was synthesized in vitro in a suspension of destroyed cells of tobacco leaves in the presence of energy sources and a small amount of nucleic acid of this virus [12].

On the basis of these experiments ~~it is thus clear that~~ it is ~~now~~ already possible to create in vitro outside the living cell several of the components of viruses. It is to be hoped that soon adequate experimental methods and substrates will be found in which components of viruses will be created as well as their integration into whole viruses.

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